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Notes:

1. Untranslatable words are replaced with asterisks (***).
2. Texts in the figures are not translated and shown as it is.

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CLAIM + DETAILED DESCRIPTION

[Claim(s)]

[Claim 1]

It has a base material and an adhesive layer which it is arranged on this base material and contains an adhesion base and pergolide, and/or its salt permitted pharmacologically, Patches which said adhesion base contains an acrylic polymer which does not have a carboxyl group and a hydroxyl group substantially in a molecule, and has self-tackiness, and a rubber system polymer, and are characterized by weight ratios of content of said acrylic polymer and content of said rubber system polymer being 1:1-1:9.

[Claim 2]

A basic nitrogen content polymer which said adhesion base contains basic nitrogen, and does not have self-tackiness is contained further, The patches according to claim 1, wherein weight ratios of the sum total of content of said acrylic polymer and said rubber system polymer and content of said basic nitrogen content polymer are 9:1-1:1.

[Claim 3]

The patches according to claim 2, wherein said basic nitrogen content polymer is at least one sort chosen from a butyl methacrylate methacrylate methacrylic acid dimethylaminoethyl copolymer and polyvinyl acetal diethylamino acetate.

[Claim 4]

Patches given in any 1 paragraph of the Claims 1-3 which said adhesive layer contains further an alicycle group saturated hydrocarbon resin system tackifier, and are characterized by weight ratios of the sum total of content of said acrylic polymer and said rubber system polymer and content of said tackifier being 1:1-1:9.

[Claim 5]

Said acrylic polymer,

A copolymer of polyacrylate and polymethyl methacrylate containing at least one sort chosen from 2-ethylhexyl acrylate, butyl acrylate, diacetone acrylamide, and tetraethylene glycol dimethacrylate,

In a 2-ethylhexyl acrylate and N-vinyl-2-pyrrolidone methacrylic acid-1,6-hexaneglycol copolymer and a row

2-ethylhexyl acrylate and a vinyl acetate copolymer

***** -- patches given in any 1 paragraph of the Claims 1-4 being one sort even if small.

[Claim 6]

Said rubber system polymer Styrene isoprene styrene block copolymer, Patches given in any 1

paragraph of the Claims 1-5 being at least one sort chosen from styrene butadiene styrene block copolymer, styrene butadiene rubber, polyisobutylene, polyisoprene rubber, and silicon rubber.

[Claim 7]

Patches given in any 1 paragraph of the Claims 1-6, wherein said rubber system polymer is styrene isoprene styrene block copolymer.

[Claim 8]

Said acrylic polymer is at least one sort chosen from a 2-ethylhexyl acrylate and N-vinyl-2-pyrrolidone methacrylic acid-1,6-hexaneglycol copolymer, and 2-ethylhexyl acrylate and a vinyl acetate copolymer, Patches given in any 1 paragraph of the Claims 1-7, wherein said rubber system polymer is styrene isoprene styrene block copolymer.

[Claim 9]

Patches given in any 1 paragraph of the Claims 1-8, wherein mesyl acid chloride of pergolide is blended with said adhesive layer.

[Claim 10]

Patches given in any 1 paragraph of the Claims 1-9, wherein said adhesive layer contains organic acids further.

[Claim 11]

The patches according to claim 10, wherein said organic acids are acetic acid and/or its salt permitted pharmacologically.

[Detailed Description of the Invention]

[0001]

[Field of the Invention]

This invention relates to patches.

In detail, it is related with the patches using pergolide.

[0002]

[Description of the Prior Art]

Although the administering method which uses a tablet, a capsule, syrups, etc. as a method of prescribing a drug for the patient is known conventionally, the method of carrying out dermal administration of the drug using patches is examined in recent years. The method of using patches can cancel the problem by the administering method, and has advantages, such as ease of reduction of frequency of administration, improvement in compliance, administration, and its stop. Therefore, it is expected as a useful medication method in case especially patients are an old man and a child.

[0003]

By the way, the corneum of the normal skin has a barrier mechanism which prevents the invasion to the inside of the body of a foreign matter. When the conventional patches are used, percutaneous absorption of the blended drugs component is not fully carried out by this barrier mechanism in many cases. Generally the skin permeability of a drug becomes remarkably low from lipophilicity of a corneum being high.

[0004]

Then, examination about the presentation etc. of the binder used for patches is advanced in order to improve the percutaneous absorption of the drug in a dermal administration method. As part of

that, the patches which used polymeric materials, such as an acrylic polymer and a rubber system polymer, for the adhesion base are proposed (JP,H4-266821,A, JP,H9-301854,A, etc.).

[0005]

[Problem to be solved by the invention]

However, even if it is a case where the above-mentioned conventional patches are used, it cannot be said that the skin permeability of a drug is not necessarily enough. In the patches of these former, if the percutaneous absorption of a drug is improved, it is very difficult to fulfill all the characteristics demanded as patches -- pharmaceutical preparation physical properties, such as the cohesiveness of an adhesive layer and tackiness, are spoiled. Although the character of the drug used for patches varies with the kind, it is one of these and the conformity of the adhesion base to a specific drug is not yet examined fully.

[0006]

This invention is made in view of the technical problem which the above-mentioned conventional technology has, and is a thing.

the purpose -- and/or, it is facing using as a drug the salt permitted pharmacologically, and providing the patches which can be attained [that it is high level and] for the both sides of the cutaneous-absorption nature of a drug, and pharmaceutical preparation physical properties.

[0007]

[Means for solving problem]

As a result of repeating research wholeheartedly that this invention persons should attain the above-mentioned purpose, many of acrylic polymers are what has a carboxyl group (-COOH) and a hydroxyl group (-OH) in the molecule as a reactive site for constructing a bridge among the polymeric materials used for the conventional patches, It found the very difficult thing that it is compatible in the skin permeability and pharmaceutical preparation physical properties of a drug using such an acrylic polymer. And in patches using pergolide and/or its salt permitted pharmacologically as a drug as a result of inquiring further based on this knowledge, By making an adhesive layer contain the acrylic polymer which does not have a carboxyl group and a hydroxyl group substantially, and has self-tackiness, and a rubber system polymer with a specific ratio, respectively, it finds out that the above-mentioned technical problem is solved, and came to complete this invention.

[0008]

Namely, the patches of this invention are provided with a base material and the adhesive layer which it is arranged on this base material and contains an adhesion base and pergolide, and/or its salt permitted pharmacologically, An adhesion base contains the acrylic polymer which does not have a carboxyl group and a hydroxyl group substantially in a molecule, and has self-tackiness, and a rubber system polymer, and it is characterized by the weight ratios of the content of an acrylic polymer and the content of a rubber system polymer being 1:1-1:9.

[0009]

"It has self-tackiness" as used in the field of this invention means that a ball stops on a film, when a polymer is fabricated in the shape of a film and a tackiness examination (a rolling ball tack test, JIS Z 0237) is done at ordinary temperature using the film.

[0010]

In the patches of this invention, the basic nitrogen content polymer which an adhesion base contains basic nitrogen and does not have self-tackiness is contained further, and it is preferred that the weight ratios of the sum total of the content of an acrylic polymer and a rubber system

polymer and the content of a basic nitrogen content polymer are 1:1-9:1.

[0011]

In the patches of this invention, it is preferred that a basic nitrogen content polymer is at least one sort chosen from a butyl methacrylate methacrylate methacrylic acid dimethylaminoethyl copolymer and polyvinyl acetal diethylamino acetate.

[0012]

In the patches of this invention, an adhesive layer contains further an alicycle group saturated hydrocarbon resin system tackifier, and it is preferred that the weight ratios of the sum total of the content of an acrylic polymer and a rubber system polymer and the content of a tackifier are 1:1-1:9.

[0013]

An acrylic polymer in the patches of this invention 2-ethylhexyl acrylate, Butyl acrylate, Diacetone acrylamide. And the copolymer of the polyacrylate and polymethyl methacrylate containing at least one sort chosen from tetraethylene glycol dimethacrylate; 2-ethylhexyl acrylate and N-vinyl-2-pyrrolidone methacrylic acid-1,6-hexaneglycol copolymer;. And it is preferred that it is at least one sort chosen from 2-ethylhexyl acrylate and a vinyl acetate copolymer.

[0014]

A rubber system polymer in the patches of this invention Styrene isoprene styrene block copolymer, It is preferred that it is at least one sort chosen from styrene butadiene styrene block copolymer, styrene butadiene rubber, polyisobutylene, polyisoprene rubber, and silicon rubber, and it is more preferred that it is styrene isoprene styrene block copolymer.

[0015]

In the patches of this invention, An acrylic polymer is at least one sort chosen from a 2-ethylhexyl acrylate and N-vinyl-2-pyrrolidone methacrylic acid-1,6-hexaneglycol copolymer, and 2-ethylhexyl acrylate and a vinyl acetate copolymer, It is preferred that a rubber system polymer is styrene isoprene styrene block copolymer.

[0016]

In the patches of this invention, it is preferred that the mesyl acid chloride of pergolide is blended with the adhesive layer.

[0017]

In the patches of this invention, it is preferred that an adhesive layer contains organic acids further, and it is more preferred that the organic acids concerned are acetic acid and/or its salt permitted pharmacologically.

[0018]

[Mode for carrying out the invention]

Hereafter, the suitable embodiment of this invention is described in detail.

[0019]

The patches of this invention are provided with a base material and the adhesive layer which it is arranged on this base material and contains an adhesion base and pergolide, and/or its salt permitted pharmacologically, An adhesion base contains the acrylic polymer which does not have a carboxyl group and a hydroxyl group substantially in a molecule, and has self-tackiness, and a rubber system polymer, and the weight ratio of the content of an acrylic polymer and the content of a rubber system polymer is a thing of 1:1-1:9.

[0020]

As a base material used for the patches of this invention, especially if an adhesive layer can be

supported, it will not be restricted, but the base material of elasticity or non-elasticity can be used. Especially, what is chosen from the textile fabrics, the nonwoven fabric, and knitted fabric which have water-vapor-permeation nature is preferred. If the base material which has water-vapor-permeation nature is used, the sweat stored between the affected part and patches at the time of pasting can be made to be able to emit effectively, and Mouret and skin irritation by sweat can be prevented. As this base material, specifically Cloth, a nonwoven fabric, polyurethane, polyester, Polypropylene, polyvinyl acetate, polyvinylidene chloride, polyethylene, The complex materials etc. of what compounded synthesis of polyethylene terephthalate, an aluminium sheet, nylon, an acrylic, cotton, rayon, acetate, etc., natural fiber, or these textiles, and was used as textile fabrics, a nonwoven fabric, and knitted fabric, and these and the film which has water-vapor-permeation nature further are mentioned. Also in these, it is preferred to use the knitted fabric made from polyester from a point of safety, flexibility, and elasticity.

[0021]

Although the thickness in particular of the base material concerning this invention is not restricted, it is preferred that it is 5-1000-micrometer-thick within the limits. It is in the trend for the work ease at the time of sticking that the thickness of a base material is less than said lower limit to fall, and when the thickness of another side and a base material exceeds said upper limit, it is in the trend for manufacture ease -- amputation of a base material or patches becomes difficult in the manufacturing process of patches -- to fall.

[0022]

In the patches of this invention, the adhesive layer by which an adhesion base and pergolide, and/or its salt permitted pharmacologically were blended on the above-mentioned base material is arranged. Here, the adhesion base concerning this invention contains the acrylic polymer (only henceforth [with a case] "an acrylic polymer") which does not have a carboxyl group and a hydroxyl group substantially in a molecule, and has self-tackiness, and a rubber system polymer.

[0023]

The acrylic polymer concerning this invention which does not have substantially a carboxyl group (a carboxylic acid group, -COOH) and a hydroxyl group (-OH) in a molecule refers to the acrylic polymer which has neither a carboxyl group which can serve as a reactive site in the case of bridge formation into the molecule, nor a hydroxyl group. Such a polymer can be obtained by polymerizing the monomer which does not have a carboxyl group and a hydroxyl group. As this monomer, methyl acrylate, ethyl acrylate, propyl acrylate, Amyl acrylate, butyl acrylate, acrylic acid-2-ethylbutyl, Hexyl acrylate, heptyl acrylate, octyl acrylate, nonyl acrylate, 2-ethylhexyl acrylate, decyl acrylate, dodecyl acrylate, tridecyl acrylate, other acrylic ester (meta) corresponding to the acrylic polymer made into the purpose, etc. are mentioned.

[0024]

As the desirable example of the acrylic polymer concerning this invention,

(A1) The copolymer of the polyacrylate and polymethyl methacrylate containing at least one sort chosen from 2-ethylhexyl acrylate, butyl acrylate, diacetone acrylamide, and tetraethylene glycol dimethacrylate

(A2) 2-ethylhexyl acrylate and N-vinyl-2-pyrrolidone methacrylic acid-1,6-hexaneglycol copolymer

(A3) 2-ethylhexyl acrylate and a vinyl acetate copolymer

*****. [as an example of goods of the acrylic polymer which does not have a carboxyl group and a hydroxyl group substantially in a molecule, and has self-tackiness] There are

DURO-TAK 87-2097 (it does not have a functional group), DURO-TAK 87-2194 (it does not have a functional group), DURO-TAK 87-4098 (it does not have a functional group), etc. which are supplied from a national starch & chemical company. If a 2-ethylhexyl acrylate and N-vinyl-2-pyrrolidone methacrylic acid-1,6-hexaneglycol copolymer, and/or 2-ethylhexyl acrylate and a vinyl acetate copolymer are used also in these, Since it is in the trend for the both sides of the skin permeability of a drug and pharmaceutical preparation physical properties to be raised more, it is more desirable. One sort may be independently used for these acrylic polymers, and may be used for them combining two or more sorts.

[0025]

If the monomer which has a carboxyl group and a hydroxyl group in a raw material monomer exists in very small quantities as an impurity in the manufacturing process of the above-mentioned acrylic polymer or side reactions, such as heat deterioration, occur in the case of a polymerization, Although the carboxyl group and hydroxyl group originating in an impurity may be introduced into the acrylic polymer obtained, Unless the skin permeability of the drug high enough which the patches of this invention have, and pharmaceutical preparation physical properties high enough are spoiled, suppose that such an acrylic polymer is included by the acrylic polymer which does not have a carboxyl group and a hydroxyl group substantially in a molecule.

[0026]

However, even if the carboxyl group and hydroxyl group in the acrylic polymer concerning this invention originate in side reactions in the manufacturing process, such as mixing of an impurity, and heat deterioration, decreasing as much as possible is preferred.

[0027]

As for the viscosity average molecular weight of the acrylic polymer concerning this invention, it is preferred that it is 200,000-1,000,000. It is in the trend for pharmaceutical preparation physical properties (especially tackiness) to fall that the viscosity average molecular weight of an acrylic polymer is less than said lower limit, and when another side and said upper limit are exceeded, it is in the trend for compatibility with other components contained in an adhesive layer to fall.

[0028]

The rubber system polymer concerning this invention refers to nature or composite elastic polymer. As the desirable example of such a rubber system polymer,

(S1) Styrene isoprene styrene block copolymer

(S2) Styrene butadiene styrene block copolymer

(S3) Styrene butadiene rubber

(S4) Polyisobutylene

(S5) Polyisoprene rubber

(S6) Silicon rubber

*****. Also in these, since it is in the trend for the both sides of the skin permeability of a drug and pharmaceutical preparation physical properties to be raised more when styrene isoprene styrene block copolymer or polyisobutylene is used, it is more desirable. One sort may be independently used for these rubber system polymers, and may be used for them combining two or more sorts.

[0029]

At least one sort chosen from a 2-ethylhexyl acrylate and N-vinyl-2-pyrrolidone methacrylic acid-1,6-hexaneglycol copolymer, and 2-ethylhexyl acrylate and a vinyl acetate copolymer as an acrylic polymer, If styrene isoprene styrene block copolymer is used as a rubber system polymer,

respectively, since the both sides of the skin permeability of a drug and pharmaceutical preparation physical properties will be raised further, it is desirable.

[0030]

As for the viscosity average molecular weight of the rubber system polymer concerning this invention, it is preferred that it is 30,000-2,500,000, and it is more preferred that it is 100,000-1,700,000. It is in the trend for pharmaceutical preparation physical properties (especially tackiness) to fall that the viscosity average molecular weight concerned is less than said lower limit, and when another side and said upper limit are exceeded, it is in the trend for compatibility with other components contained in an adhesive layer to fall.

[0031]

In this invention, the weight ratio of the content of the acrylic polymer which does not have a carboxyl group and a hydroxyl group substantially in a molecule, and the content of a rubber system polymer needs to be within the limits of 1:1-1:9. When the pergolide and/or its salt permitted pharmacologically as a drug are blended with an adhesive layer by carrying out the weight ratio of both content said within the limits, the skin permeability of the drug concerned improves remarkably, and achievement of high level pharmaceutical preparation physical properties is attained. By carrying out the weight ratio of both content said within the limits, moderate adhesive power is given to an adhesive layer and stickiness and skin irritation are improved. The skin permeability of a drug becomes that the content of a rubber system polymer is less than 1 time of the content of an acrylic polymer insufficient. If the content of a rubber system polymer exceeds 9 times of the content of an acrylic polymer, pharmaceutical preparation physical properties will become insufficient.

[0032]

[the content of the acrylic polymer concerning this invention] Especially if the weight ratio to the content of a rubber system polymer is said within the limits, it will not be restricted, but it is preferred that it is 0.2 to 60 weight % on the basis of the adhesion base whole quantity, it is more preferred that it is 0.5 to 50 weight %, and it is still more preferred that it is 1 to 40 weight %. It is in the trend for the skin permeability of a drug to fall that the loadings of an acrylic polymer are less than said lower limit, and when another side and said upper limit are exceeded, it is in the trend for the force of coagulation of an adhesive layer to decline.

[0033]

[the loadings of the rubber system polymer concerning this invention] Especially if the weight ratio to the content of an acrylic polymer is said within the limits, it will not be restricted, but it is preferred that it is 0.2 to 60 weight % on the basis of the adhesion base whole quantity, it is more preferred that it is 0.5 to 50 weight %, and it is still more preferred that it is 1 to 40 weight %. The skin permeability of a drug falls that the loadings of a rubber system polymer are less than said lower limit. "it is in a trend, and when another side and said upper limit are exceeded, it is in the trend for the adhesive power of an adhesive layer to decline.

[0034]

As for the adhesion base concerning this invention, it is preferred to contain further the basic nitrogen content polymer (only henceforth "a basic nitrogen content polymer") which contains basic nitrogen and does not have self-tackiness in addition to the above-mentioned acrylic polymer and a rubber system polymer. By making an adhesion base contain a basic nitrogen content polymer, the solubility of a drug and pharmaceutical preparation physical properties can be raised further. Therefore, when pergolide and/or its salt permitted pharmacologically are blended with an adhesive layer, the phenomenon in which these drugs crystallize and deposit is

prevented more certainly, and it is equal also to long-term preservation, and cutaneous-absorption nature is good and the patches by which a medicinal value is demonstrated continuously for a long time become realizable.

[0035]

As this basic nitrogen content polymer, the polymer which has functional groups, such as an amino group, an amide group, an imino group, and an imido group, can be used. When a basic nitrogen content polymer has an amino group, the amino groups concerned may be any of the 1st class, the 2nd class, and the 3rd class. When an amino group is the 2nd class or the 3rd class, a substituted alkyl group may be a chain or may form the ring.

[0036]

As such a basic nitrogen content polymer, acrylic acid (meta) dimethylaminoethyl, (Meta) The homopolymer of polymerization nature amine, such as acrylic acid (meta) dialkylamino alkyls, such as diethylaminoethyl acrylate, and vinyl pyrrolidone, or these two or more sorts of copolymers, Polyvinyl dialkylamino acetate, such as a copolymer of one sort of the above-mentioned polymerization nature amine or two sorts or more, and the monomer in which other polymerizations are possible, and polyvinyl acetal diethylamino acetate, etc. are mentioned.

[0037]

As polymerization nature amine and a monomer which can be polymerized, methyl acrylate, ethyl acrylate, Propyl acrylate, butyl acrylate, isobutyl acrylate, hexyl acrylate, Octyl acrylate, 2-ethylhexyl acrylate, decyl acrylate, Acrylic acid isodecyl, acrylic acid lauryl, stearyl acrylate, Methyl methacrylate, ethyl methacrylate, butyl methacrylate, isobutyl methacrylate, methacrylic acid-2-ethylhexyl, decyl methacrylate, methacrylic acid isodecyl, lauryl methacrylate, stearyl methacrylate, etc. are mentioned.

[0038]

If at least one sort chosen from a butyl methylmethacrylate methacrylate methacrylic acid dimethylaminoethyl copolymer and polyvinyl acetal diethylamino acetate is used also in an above-mentioned basic nitrogen content polymer, Since it is more excellent and can be compatible in the skin permeability and pharmaceutical preparation physical properties of a drug, it is desirable. as a butyl methylmethacrylate methacrylate methacrylic acid dimethylaminoethyl copolymer -- OI DORAGITTOE (a trade name.) Made in Rehm etc. can use commercial items, such as AEA (a trade name, the Sankyo [Co., Ltd.] Co., Ltd. make), as polyvinyl acetal diethylamino acetate.

[0039]

As for the viscosity average molecular weight of a basic nitrogen content polymer, it is preferred that it is 100,000-5,000,000, and it is more preferred that it is 1,000,000-3,000,000. When the viscosity average molecular weight of a basic nitrogen content polymer is in the trend which becomes insufficient [the addition effect (especially cohesiveness) of a basic nitrogen content polymer] for it to be less than said lower limit and exceeds another side and said upper limit, it is in the trend for compatibility with other components contained in an adhesive layer to fall.

[0040]

Although the content in particular of the basic nitrogen content polymer in an adhesion base is not restricted, it is preferred that the weight ratios of the sum total of the content of an acrylic polymer and a rubber system polymer and the content of a basic nitrogen content polymer are 9:1-1:1. It is in the trend for the skin permeability improvement effect of the drug according that the content of a basic nitrogen content polymer is less than [of the sum total of the content of an acrylic polymer and a rubber system polymer] 1/9 to a basic nitrogen content polymer to fall.

When the content of a basic nitrogen content polymer exceeds 1 time of the sum total of the content of an acrylic polymer and a rubber system polymer, it is in the trend for the tackiness of an adhesive layer to fall.

[0041]

As for the content of the basic nitrogen content polymer in an adhesion base, it is preferred that it is 1 to 30 weight % on the basis of the adhesion base whole quantity, and it is more preferred that it is 5 to 20 weight %. It is in the trend for the skin permeability of a drug to fall that the content of a basic nitrogen content polymer is less than said lower limit, and when another side and said upper limit are exceeded, it is in the trend for the tackiness of an adhesive layer to fall.

[0042]

In this invention, unless the skin permeability and pharmaceutical preparation physical properties of a drug are spoiled, in an adhesive layer, rubber system polymers, such as an ethylene-vinyl acetate copolymer (EVA, content of vinyl acetate: 5 to 60 weight %), may be contained further. As for the content of this rubber system polymer, 0.05 to 1 weight % is preferred on the basis of the compound whole quantity contained in an adhesive layer.

[0043]

In the patches of this invention, pergolide and/or its salt permitted pharmacologically are blended with an adhesive layer as an active principle. When blending the salt with which pergolide is permitted pharmacologically, the salt may be any of mineral salt and organic salt, but especially mesyl acid chloride (namely, pergolide mesilate) is preferred.

[0044]

In this invention, as for pergolide and/or its loadings of a salt permitted pharmacologically, it is preferred that it is 0.1 to 50 weight % on the basis of the compound whole quantity contained in an adhesive layer, and it is more preferred that it is 1 to 20 weight %. It is in the trend for the skin permeability of a drug to fall that pergolide and/or its loadings of a salt permitted pharmacologically are less than said lower limit. On the other hand, when the loadings concerned exceed said upper limit, pergolide and/or its salt permitted pharmacologically may crystallize and deposit, without the ability to dissolve in an adhesive layer, and it is in the trend for physical properties to fall.

[0045]

Although the adhesive layer concerning this invention contains an above-mentioned adhesion base and drug, in addition to these components, it may contain a tackifier further. [as a tackifier used in this invention] concrete -- a rosin derivative (the glycerol ester of rosin and rosin.) The glycerol ester of ***** rosin and ***** rosin, penta ERIS torr ester of rosin, etc., Alicycle group saturated hydrocarbon resin (Al Cong P100 (made by Arakawa Chemical Industries, Ltd.) etc.), aliphatic series system hydrocarbon resin (Quinton B-170 (made by Nippon Zeon Co., Ltd.) etc.), terpene resin (KURIARON P-125 (made by Yasuhara Chemical) etc.), maleic acid resin, etc. are mentioned. Also in these, the glycerol ester of ***** rosin, aliphatic series system hydrocarbon resin, and terpene resin are preferred, and especially alicycle group saturated hydrocarbon resin is preferred.

[0046]

Although the loadings in particular of the tackifier concerning this invention are not restricted, it is preferred that it is 5 to 70 weight % on the basis of the compound whole quantity contained in an adhesive layer, it is more preferred that it is 5 to 60 weight %, and it is still more preferred that it is 10 to 50 weight %. When the loadings of a tackifier are in the trend which becomes insufficient [the adhesive power improvement effect of patches according that it is less than said

lower limit to combination of a tackifier] and exceed another side and said upper limit, it is in the trend for the skin irritation at the time of exfoliating to increase patches.

[0047]

When using alicycle group saturated hydrocarbon resin as a tackifier, it is preferred that the weight ratios of the sum total of the content of an acrylic polymer and said rubber system polymer and the content of a tackifier are 1:1-1:9. If the conditions of the above [each content of an acrylic polymer, a rubber system polymer, and a tackifier] are fulfilled, the patches by which the both sides of pergolide, and/or its skin permeability of a salt permitted pharmacologically and pharmaceutical preparation physical properties were raised more, adhesive power was further heightened more, and stickiness and skin irritation have been improved further will be obtained.

[0048]

In this invention, it is preferred that an adhesive layer contains organic acids further. as these organic acids -- aliphatic series (mono- ** II or bird) carboxylic acid (acetic acid.) Propionic acid, citric acid (anhydrous citric acid is included), isobutyric acid, caproic acid, Caprylic acid, lactic acid, maleic acid, pyruvic acid, oxalic acid, succinic acid, aromatic carboxylic acid (phthalic acid, salicylic acid, and benzoic acid.), such as tartaric acid alkyl sulfonic acid (methanesulfonic acid.), such as acetylsalicylic acid Ethane sulfonic acid, propylsulfonic acid, butanesulfonic acid, polyoxyethylene-alkyl-ether sulfonic acid, etc., Alkyl-sulfonic-acid derivative (N-2-hydroxyethyl piperidine- N'-2-ethane sulfonic acid, call acid derivatives (dehydrocholic acid etc.), or these salts (for example, alkali metal salt, such as sodium salt) are mentioned.) Also in these organic acids, carboxylic acid and these salts are preferred, and acetic acid, sodium acetate, and especially citric acid are preferred. One sort may be independently used for these organic acids, and may be used for them combining two or more sorts.

[0049]

In the adhesive layer concerning this invention, although the content in particular of organic acids is not restricted, it is preferred that it is 0.01 to 20 weight % on the basis of the compound whole quantity contained in an adhesive layer, it is more preferred that it is 0.1 to 15 weight %, and it is still more preferred that it is 0.1 to 10 weight %. When the content of an organic acid becomes insufficient [the skin permeability improvement effect of the drug according that it is less than said lower limit to an organic acid] and exceeds another side and said upper limit, it is in the trend which skin irritation increases.

[0050]

The adhesive layer concerning this invention may contain absorption enhancers further. As this absorption enhancers, can use the compound in which the absorption promotion operation on the skin is accepted conventionally, and specifically, Fatty acid, fatty alcohol, fatty acid ester, amide or ether, an aromatic organic acid, aromatic alcohol, aromatic organic acid ester, or ether of the carbon numbers 6-20, etc. is mentioned. These compounds may be saturation and unsaturated any, and straight chain shape, the letter of branching, and annular any may be sufficient as them. In this invention, lactate, acetate, a monoterpene system compound, A sesquiterpene system compound, EIZON (Azone), an EIZON (Azone) derivative, Glycerine fatty acid ester, propylene glycol fatty acid ester, Sorbitan fatty acid ester (Span system), a polysorbate series compound (Tween system), Polyethylene glycol fatty acid ester, a polyoxyethylene hydrogenated-castor-oil system compound (HCO system), polyoxyethylene alkyl ether, sucrose fatty acid ester, a vegetable oil, etc. can be used as absorption enhancers. Also in such absorption enhancers, caprylic acid, capric acid, caproic acid, Lauric acid, myristic acid, palmitic acid, stearic acid, isostearic acid, Oleic acid, linolic acid, linolenic acid, lauryl alcohol, myristyl alcohol, Oleyl

alcohol, isostearyl alcohol, cetyl alcohol, Methyl laurate, hexyl laurate, lauric acid diethanolamide, Isopropyl myristate, myristic acid Millis Chill, myristic acid octyldodecyl, The cetyl palmitate, salicylic acid, methyl salicylate, ethylene glycol salicylate, Cinnamic acid, methyl cinnamate, cresol, lactic acid Sept Iles, lactic acid lauryl, Ethyl acetate, propyl acetate, geraniol, Timor, eugenol, Terpeneol, l-menthol, the Borneo roll, d-limonene, Isoeugenol, isoborneol, Nellore, dl-camphor, A glycerol mono- KAPURI rate, glycerol mono- caprate, glycerine monolaurate, glycerol monooleate, sorbitan monolaurate, cane sugar mono- laurate, the polysorbate 20, propylene glycol, propylene glycol mono- laurate, Polyethylene glycol monolaurate, polyethylene glycol monostearate, Polyoxyethylene lauryl ether, HCO-60, PIROCHIO decane, Olive oil's is preferred and Lauryl alcohol, myristyl alcohol, Isostearyl alcohol, lauric acid diethanolamide, a glycerol mono- KAPURI rate, Glycerol mono- caprate, glycerol monooleate, sorbitan monolaurate, propylene glycol mono- laurate, polyoxyethylene lauryl ether, and PIROCHIO decane are more preferred. One sort may be independently used for such absorption enhancers, and may be used for it combining two or more sorts.

[0051]

In the adhesive layer concerning this invention, although the content in particular of absorption enhancers is not restricted, it is preferred that it is 0.01 to 20 weight % on the basis of the compound whole quantity contained in an adhesive layer, it is more preferred that it is 0.05 to 10 weight %, and it is still more preferred that it is 0.1 to 5 weight %. When the content of absorption enhancers is in the trend which becomes insufficient [the skin permeability improvement effect of the drug according that it is less than said lower limit to absorption enhancers] and exceeds another side and said upper limit, it is in the trend which the stimulativeness to the skins, such as an edema, increases.

[0052]

The adhesive layer concerning this invention may contain a plasticizer further. as this plasticizer -- concrete -- petroleum system oil (paraffin series process oil.) Squalane, such as naphthene system process oil and aromatic system process oil, squalene and vegetable system oil (olive oil, camellia oil, castor oil, and tall oil.) Peanut oil, a silicone oil, liquid rubber (polybutene, liquid isoprene rubber), liquid-fatty-acid ester (isopropyl myristate and hexyl laurate.) Diethylene glycol, such as diethyl sebacate and diisopropyl sebacate, polyethylene glycol, propylene glycol, dipropylene glycol, triacetin, triethyl citrate, crotamiton, etc. are mentioned. Also in these plasticizers, liquid paraffin, liquefied polybutene, crotamiton, diethyl sebacate, and especially hexyl laurate are preferred. One sort may be independently used for these plasticizers, and may be used for them combining two or more sorts.

[0053]

In the adhesive layer concerning this invention, although the content in particular of a plasticizer is not restricted, it is preferred that it is 5 to 70 weight % on the basis of the compound whole quantity contained in an adhesive layer, it is more preferred that it is 10 to 60 weight %, and it is still more preferred that it is 10 to 50 weight %. When the content of a plasticizer is in the trend which becomes insufficient [the force-of-coagulation improvement effect of patches according that it is less than said lower limit to combination of a plasticizer] and exceeds another side and said upper limit, it is in the trend which becomes insufficient [the skin permeability of a drug].

[0054]

An adhesive layer can be made to contain an anti-oxidant, a bulking agent, an ultraviolet ray absorbent, etc. in this invention if needed.

[0055]

As an anti-oxidant concerning this invention, tocopherol and these ester derivatives, ascorbic acid, L-ascorbyl stearate, NORUJIHITORO guaiaretic acid, dibutylhydroxytoluene (BHT), and butylhydroxyanisole are preferred.;

As a bulking agent, calcium carbonate, magnesium carbonate, silicate (for example, aluminium silicate, magnesium silicate, etc.), silicic acid, barium sulfate, calcium sulfate, calcium plumbite, zinc oxide, and titanium oxide are preferred.;

As an ultraviolet ray absorbent, a p-aminobenzoic acid derivative, an anthranilic acid derivative, salicylic acid derivatives, a coumarin derivative, an amino acid system compound, an imidazoline derivative, a pyrimidine derivative, and a dioxane derivative are preferred.

[0056]

Although each content in particular of an anti-oxidant, a bulking agent, and an ultraviolet ray absorbent is not restricted, in the adhesive layer concerning this invention, [the sum total of the content of an anti-oxidant a bulking agent, and an ultraviolet ray absorbent] It is preferred that it is 0 to 10 weight % on the basis of the compound whole quantity contained in an adhesive layer, it is more preferred that it is 0 to 5 weight %, and it is still more preferred that it is 0 to 2 weight %.

[0057]

Although it faces forming the adhesive layer which has the above-mentioned composition on a base material and the formation method in particular is not restricted, For example, the patches of this invention can be obtained by carrying out the thermal melting solution of the mixture of a component besides the above added an adhesion base, pergolide and/or its salt permitted pharmacologically, and if needed, and coating to a base material. When the patches of this invention are further provided with a release paper on an adhesive layer, After coating the above-mentioned mixture which pasted the base material together on the coating surface, or carried out the thermal melting solution after coating the above-mentioned mixture which carried out the thermal melting solution to a release paper to a base material, the patches of this invention can be obtained by pasting a releasing paper together on a coating surface. The patches of this invention can be obtained also by using the coating liquid in which solvents, such as toluene, hexane, and ethyl acetate, were made to dissolve the above-mentioned mixture instead of carrying out the thermal melting solution of the above-mentioned mixture.

[0058]

The patches of this invention may be provided with the adhesive layer of one layer, and unless pergolide and/or its skin permeability of a salt permitted pharmacologically are spoiled, they may be provided with the adhesive layer more than two-layer.

[0059]

Although the thickness in particular of the adhesive layer concerning this invention is not restricted, it is preferred that it is 20-200 micrometers. It is in the trend which becomes insufficient [the skin permeability of a drug] for the thickness of an adhesive layer to be less than said lower limit, and is in the trend for the phenomenon (binder remainder) which remains while the binder had adhered to the skin after pasting, when another side and said upper limit were exceeded to happen easily.

[0060]

When the patches of this invention are provided with a release paper, specifically as this release paper, films, such as polyester, such as polyethylene terephthalate, polyvinyl chloride, and polyvinylidene chloride, the laminate film of paper of fine quality and polyolefine, etc. are mentioned. In these releasing papers, if it siliconizes to the field of the side in contact with an

adhesive layer, since the work ease at the time of exfoliating a release paper from patches will be improved, it is desirable.

[0061]

[Working example]

Hereafter, although this invention is explained still more concretely based on an embodiment and a comparative example, this invention is not limited to the following embodiments at all.

[0062]

[Embodiment 1]

Pergolide mesilate, acetic acid, sodium acetate, sorbitan monolaurate, isostearyl alcohol, and liquid paraffin were taken to the mortar, and it fully mixed. This mixture 2-ethylhexyl acrylate and a vinyl acetate copolymer (polymer (A)), Styrene isoprene styrene block copolymer (polymer (B)), In addition to the mixed liquor which consists of a butyl methylmethacrylate methacrylate methacrylic acid dimethylaminoethyl copolymer (OIDORAGITTOE, polymer (C)), alicycle group saturated hydrocarbon resin, heptane, and ethyl acetate, the coating liquid for adhesive layers was prepared. The sum total of the content (value on the basis of the compound whole quantity except heptane and ethyl acetate) of each component in the obtained coating liquid and the content of a polymer (A) and (B) and the weight ratio of the content of a polymer (A) and the content of a polymer (B) are shown in Table 1. In this example and Embodiments 2-6 mentioned later, and the comparative examples 1-10, the content (5.0 weight %) of a surface active agent means the content of the sum total of sorbitan monolaurate (2.0 weight %) and isostearyl alcohol (3.0 weight %).

[0063]

Next, the obtained coating liquid was applied on the release paper made from polyethylene terephthalate, dry elimination of the solvent was carried out, and the adhesive layer was formed. The knitted fabric made from polyester as a base material was pasted together to the adhesive layer, and the target patches were obtained.

[0064]

[Embodiments 2 and 3, the comparative examples 1 and 2]

In Embodiments 2 and 3 and the comparative examples 1 and 2, patches were produced like Embodiment 1 except having carried out as the content of 2-ethylhexyl acrylate, a vinyl acetate copolymer, and styrene isoprene styrene block copolymer was shown in Tables 1 and 2, respectively.

[0065]

[Embodiments 4-6, the comparative examples 3 and 4]

In Embodiments 4-6 and the comparative examples 3 and 4, not using the butyl methylmethacrylate methacrylate methacrylic acid dimethylaminoethyl copolymer, patches were produced like Embodiment 1 except having carried out, respectively as the presentation of the coating liquid for adhesive layers was shown in Tables 1 and 2.

[0066]

[Comparative examples 5-10]

The acrylic polymer (DURO-TAK 87-2852) which has the acrylic polymer (DURO-TAK 87-2287) or carboxyl group which has a hydroxyl group instead of in the comparative examples 5-10, respectively is used, [2-ethylhexyl acrylate and a vinyl acetate copolymer] Patches were produced except having carried out like Embodiment 1 as the presentation of the coating liquid for adhesive layers was shown in Tables 2 and 3.

[0067]

(Skin permeability examination)

The following examinations were done using each patches obtained by Embodiments 1-6 and the comparative examples 1-10.

[0068]

First, the hairless mouse regions-of-back skin was exfoliated, and the flow through cell which made the peripheral part circulate through 37 °C warm water was equipped by using the dermis side as the receptor side layer. Next, stick patches (5 cm of pharmaceutical preparation application surface product ²) on the corneum side of the skin, sample a receptor solution every 2 hours by 5 ml/hr till 24 hours, using a physiological saline as a receptor layer, and measure the flow rate, and. The drug level was measured using high performance chromatography. The drug transmission rate per hour was computed from the acquired measured value, and it asked for the drug transmission rate per unit area of the skin in a stationary state. The maximum (the maximum skin transmission rate) of the drug transmission rate obtained from the start of test before 24 hours is shown in Tables 1-3.

[0069]

(Pharmaceutical preparation physical-properties examination)

About each patches of Embodiments 1-6 and the comparative examples 1-10, the tackiness, cohesiveness, and stability of the adhesive layer were evaluated. The adhesive evaluation test was done with the probe tackiness tester and the peel testing machine. The coherent evaluation test was done with the creep measurement machine. Doing an above-mentioned adhesive evaluation examination about the patches saved for six months at 40 °C estimated stability. Evaluations of these pharmaceutical preparation physical properties are the following bases. :

A: It is very good.

B: It is good.

C: It is bad.

It was alike and carried out by being based. The obtained result is shown in Tables 1-3.

[0070]

[Table 1]

		実施例 1	実施例 2	実施例 3	実施例 4	実施例 5	実施例 6
組成 [重量%]	(A)	アクリル酸-2-エチルヘキシル ・酢酸ビニル共重合体					
	(B)	スチレン-イソブレン-ブタジエン共重合体					
	(C)	メタアクリル酸メチル・メタアクリル酸ブチル ・メタアクリル酸ジメチルアミエチル 共重合体					
	脂環族炭化水素樹脂		40.0	40.0	40.0	40.0	40.0
	流動パラフィン		15.0	15.0	15.0	15.0	15.0
	酢酸ナトリウム		1.8	1.8	1.8	1.8	1.8
	酢酸		5.3	5.3	5.3	5.3	5.3
	界面活性剤		5.0	5.0	5.0	5.0	5.0
	ジアルコキシシリケート		9.0	9.0	9.0	9.0	9.0
	(A), (B) の合計 [重量%]		14.3	14.3	14.3	23.9	23.9
(A) と (B) との重量比		1:9	3:7	5:5	1:9	3:7	5:5
最大皮膚透過速度 [$\mu\text{g}/\text{cm}^2/\text{hr}$]		19.6	17.0	14.8	8.6	7.0	6.0
製剤物性	粘着性	B	A	A	B	A	A
	凝集性	B	A	A	B	A	A
	安定性	A	A	A	A	A	A

[0071]
[Table 2]

[0072]

組成		比較例 1	比較例 2	比較例 3	比較例 4	比較例 5
[重量%]	(A)	アクリル酸-2-エチルヘキシル ・酢酸ビニル共重合体				
	(B)	14.3	4.3	23.9	7.2	12.8
	(C)	9.6	9.6	-	-	9.6
	(D)	スチレン-イソブレン-スチレン共重合体 メタアクリル酸メチル・メタアクリル酸ブチル ・メタアクリル酸ジメチルアミノエチル 共重合体				
		-	-	-	-	-
	脂環族炭化水素樹脂	DURO-TAK87-2287				
		-	-	-	-	1.4
	流動パラフィン	40.0	40.0	40.0	40.0	40.0
		15.0	15.0	15.0	15.0	15.0
	酢酸ナトリウム	1.8	1.8	1.8	1.8	1.8
製剤物性	酢酸	5.3	5.3	5.3	5.3	5.3
	界面活性剤	5.0	5.0	5.0	5.0	5.0
	メシル酸ベリゴリド [®]	9.0	9.0	9.0	9.0	9.0
	(A), (B) の合計[重量%]	14.3	14.3	23.9	23.9	22.4
	(A) と (B) との重量比	0:10	7:3	0:10	7:3	0:10
	最大皮膚透過速度 [$\mu\text{g}/\text{cm}^2/\text{hr}$]	14.0	8.6	4.0	3.6	7.0
	粘着性	C	B	C	B	B
	凝集性	C	C	C	C	C
	安定性	-	-	-	-	-

[Table 3]

		比較例 6	比較例 7	比較例 8	比較例 9	比較例 10
組成 [重量%]	(A)	-	-	-	-	-
	(B)	10.0	7.15	12.9	10.0	7.15
	(C)	9.6	9.6	9.6	9.6	9.6
	(D)	-	-	1.4	4.3	7.15
		4.3	7.15	-	-	-
		40.0	40.0	40.0	40.0	40.0
		15.0	15.0	15.0	15.0	15.0
		1.8	1.8	1.8	1.8	1.8
		5.3	5.3	5.3	5.3	5.3
		5.0	5.0	5.0	5.0	5.0
		9.0	9.0	9.0	9.0	9.0
(A), (B)の合計[重量%]		10.0	7.15	12.9	10.0	7.15
(A)と(B)との重量比		0:10	0:10	0:10	0:10	0:10
最大皮膚透過速度[$\mu\text{g}/\text{cm}^2/\text{hr}$]		4.4	3.0	8.6	6.6	5.0
製剤物性	粘着性	C	C	B	C	C
	凝集性	C	C	C	C	C
	安定性	-	-	-	-	-

[0073]

[Effect of the Invention]

According to this invention, in patches using pergolide and/or its salt permitted pharmacologically as a drug, it becomes possible to be excellent and to attain the both sides of the cutaneous-absorption nature of a drug, and pharmaceutical preparation physical properties as explained above.

[Translation done.]